Optimal tattoo removal in a single laser session based on the method of repeated exposures

Theodora Kossida, MD, PhD,[a] Dimitrios Rigopoulos, MD, PhD,[a] Andreas Katsambas, MD, PhD,[a] and R. Rox Anderson, MD[b]
Athens, Greece, and Boston, Massachusetts

Background: Unwanted tattoos are treated with Q-switched lasers. Despite a series of treatments, efficacy is limited.

Objective: We compared a single Q-switched laser treatment pass with 4 treatment passes separated by 20 minutes.

Methods: Eighteen tattoos on 12 adults were divided in half and randomized. One half received a single treatment pass (the "conventional" method) with a Q-switched alexandrite laser (5.5 J/cm^2, 755 nm, 100-nanosecond pulse duration, 3-mm spot size), and the other half received 4 treatment passes with an interval of 20 minutes between passes (the "R20" method). Tattoo lightening was compared 3 months later, by blinded evaluation of photographs. Biopsy specimens obtained before and immediately after treatment on both halves were also compared in blinded fashion.

Results: Immediate whitening reaction occurred on the first treatment pass, with little or no whitening on subsequent passes. Three months later, treatment with the R20 method was much more effective than conventional single-pass laser treatment ($P < .01$; all tattoos favored the R20 method). Despite greater epidermal injury with the R20 method, neither method caused adverse events or scarring. Light microscopy showed greater dispersion of tattoo ink with the R20 method.

Limitations: This prospective study involved a small number of subjects.

Conclusions: The R20 method is much more effective than conventional laser tattoo treatment, removing most tattoos in a single treatment session. New laser device technology is not required to practice this method. (J Am Acad Dermatol 2012;66:271-7.)

Key words: efficacy; laser; multiple exposure; Q-switched; removal; tattoo.

INTRODUCTION

Q-switched lasers emitting short, high-intensity pulses are widely used for treatment of unwanted tattoos based on the principles of selective photothermolysis.[1-6]

Multiple treatment sessions (4-6 for amateur tattoos and up to 20 for professional tattoos) are usually necessary to obtain acceptable tattoo lightening.[7-10] The number of treatment sessions depends on pigment color, composition, density, depth, duration, body location, and the number of tattoo inks present. Each successive treatment removes some of the remaining pigment.[7,8,11] Laser treatment fragments the tattoo ink particles, which are then cleared or

From the 1st Department of Dermatology, Andreas Sygros Hospital, National and Kapodistrian University of Athens Medical School, Athens,[a] and Wellman Center for Photomedicine, Department of Dermatology, Massachusetts General Hospital, Harvard University Medical School, Boston.[b]

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Correspondence to: Theodora Kossida, MD, PhD, 5, I. Dragoumi Street, 16121 Athens, Greece (temporary). E-mail: thkossida@gmail.com.

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rephagocytosed into smaller aggregations to the point where the tattoo is no longer clinically apparent.[5,12-14] Laser treatments are typically spaced 1 to 2 months apart.[4,7,15] The overall treatment course is often prolonged, costly, and sometimes impractical, which can lead to patient dissatisfaction and abandonment of the treatment.[2,9,11,16] Risks of treatment include scarring,[2] permanent hypopigmentation,[15,16] and the possibility of incomplete tattoo removal.[13] For these reasons, laser tattoo removal frustrates patients and challenges clinicians.

In a preliminary animal (swine) study, we compared the efficacy of tattoo removal by using a wide range of pulse durations and treatment conditions. A surprising result was that administration of multiple laser exposures delivered after fading of the immediate whitening reaction was more effective than a single laser exposure. Immediate whitening is a common reaction to Q-switched laser treatment due to bubbles that form in the dermis. The immediate whitening reaction fades over about 20 minutes, as the gas bubbles dissolve. We decided to compare the efficacy of Q-switched laser tattoo removal in a single pass versus treatment in multiple passes with a 20-minute interval between them. The cumulative effect of two consecutive pulses delivered one immediately after another has been previously examined and appeared to offer only slightly greater efficacy.[17] The administration of two pulses separated by 30 seconds to 20 minutes has also been tested and was not more effective than one pulse.[6] We hypothesized that the temporary increase in optical scattering due to immediate whitening reaction[4] limits penetration and efficacy of laser treatment, such that a second exposure performed before fading of the immediate whitening reaction did not substantially improve efficacy.

CAPSULE SUMMARY

- Tattoo removal by Q-switched lasers is generally safe and effective, but many treatment sessions are needed and residual tattoo ink often remains.
- This article shows that tattoo removal is much more effective when 4 laser "passes" are given about 20 minutes apart. Most tattoos were removed in a single session.
- Without any new laser technology, dermatologists can provide better and more efficient treatment.

MATERIALS AND METHODS

Subjects

This human study was performed in compliance with institutional ethical review standards in Greece. Twelve healthy Caucasians with a total of 8 professional and 10 amateur tattoos (Table I) were recruited either through outpatient screening or through postings at tattoo parlors. Patients with infections, coagulopathy, photosensitivity, or immunocompromise were excluded. Informed consent was obtained from all participants. Tattoo location was variable, and size ranged from 10 to 150 cm^2. Amateur tattoos were black. Three professional tattoos contained green pigment and two had small areas of blue pigment. Three amateur tattoos had been re-tattooed and contained an excessive amount of pigment. One patient with an amateur tattoo had previously undergone dermabrasion, which resulted in a hypopigmented, hypertrophic scar. None of the patients had a history of keloid formation.

Treatment procedure

Each tattoo was divided into two approximately equal parts, which were randomized for treatment with either (1) "conventional" method using a single laser pass or (2) "R20" method using 4 consecutive passes separated by 20 minutes.

All tattoos were treated by the same investigator, with a Q-switched alexandrite laser (755-nm wavelength; 3-mm uniform beam diameter; 100-nanosecond pulse duration; fluence 5.5 J/cm^2) (Cynosure, Westford, MA), delivered at 1 Hz in a minimally overlapping manner (10%-15% of the beam diameter). EMLA anesthetic cream (AstraZeneca, London, UK) was applied under occlusion for 90 to 120 minutes before treatment. If requested by the patient, 1% lidocaine was injected subcutaneously between exposures. After laser treatment, sodium fusidate ointment (with betamethasone valerate in case of severe erythema) was applied. Neomycin with bacitracin was applied to biopsied sites. After-treatment care was twice-daily cleansing and antibiotic ointment for 5 days and sun avoidance for 3 months. Patients were followed up for 6 months and completed a questionnaire regarding satisfaction and tolerance.

Evaluations of response

Subjects were examined and standardized digital color photographs were taken before, immediately after, and 3 months after treatment. Two dermatologists unaware of the treatment protocol simultaneously and independently assessed tattoo lightening from digital photographs by using a previously established 5-point scale: 1 = 0-25% (none or slight lightening), 2 = 26%-50% (moderate), 3 = 51%-75% (significant),

Table I. Patient demographics (N = 12)

Age group	No. of patients (N = 12)	No. of patients w/professional tattoos (N = 6)*	No. of patients w/amateur tattoos (N = 8)*	Sex	No. of patients	Skin phototype	No. of patients
18-24	2	1	1	Male	10	I	—
25-29	2	2	—	Female	2	II	1
30-39	5	2	4			III	7
40-49	3	1	3			IV	4
50-64	—	—	—			V	—
64+	—	—	—			VI	—

w/, With; —, none.
*Two patients had both professional and amateur tattoos.

4 = 76%-95% (very good), 5 = 96%-100% (excellent). A Wilcoxon matched-pair signed-rank test was used to compare the outcome of the two treatment methods. Qualitative end points included presence of blisters, scaling, sloughing, textural changes, hyperpigmentation, hypopigmentation, and inflammation, graded as: I (absent), II (mild), III (moderate), and IV (severe).

Histologic evaluation

Punch biopsies 3 or 4 mm in diameter were performed in all patients before and immediately after laser treatment on both halves of the tattoo, processed and embedded in paraffin, cut and stained with hematoxylin-eosin. Ten 5-μm sections per block were evaluated in a blinded fashion by two expert independent dermatopathologists, who estimated dermal pigment content and depth on a scale of 1 to 4 representing 0-25%, 26%-50%, 51%-75%, and 76%-100% decrease in pigment. Evidence of inflammation was recorded. Epidermal and dermal changes were graded as follows: absent, mild, moderate, or extensive.

RESULTS

Clinical evaluation

Treatment sessions lasted 70 to 90 minutes due to waiting 20 minutes between passes on the R20 side. An average of 236 pulses was delivered on each tattoo, ranging from 117 to 680 pulses. Some patients experienced mild pain whereas others needed anesthetic administration between subsequent exposures. Pain was greater with darker skin and/or denser tattoo pigment. There was no difference in pain per pass, associated with single-pass or multiple-pass treatments.

Slightly raised, ash-white papules appeared immediately after the first laser exposure of tattooed skin, corresponding each exactly to the laser spot (Fig 1, *A*). The immediate whitening response faded away within 20 minutes. Immediately after the subsequent R20 laser exposures, there was little or no whitening. Some tattoos appeared lighter upon completion of the R20 method (Fig 1, *B*).

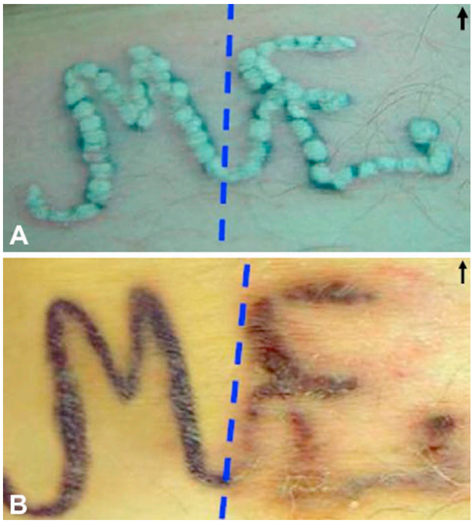

Fig 1. Amateur tattoos immediately after first and fourth consecutive laser exposures. **A**, After first exposure, immediate whitening is seen. **B**, After fourth exposure, immediate whitening is not seen, and the tattoo appears somewhat lighter.

There was no gross bleeding, tissue splattering, or loss of epidermis, but small blisters, punctate hemorrhages, purpuric macules, and transient inflammatory changes were observed. All patients tolerated treatment well. A scale-crust formed on both halves, which sloughed within 2 weeks. The residual tattoos then gradually faded over 6 to 10 weeks.

With the R20 method, most (61%) of the tattoo sites cleared completely (score 5). Five of the 8 professional tattoos (63%), and 6 of the 7 amateur tattoos (86%) cleared completely in the half treated with the R20 method. The average lightening, scored by blinded evaluation, for professional tattoos treated with the R20 method was 88%. The average lightening for amateur tattoos was 84%, which increased to 96% if the 3 re-tattooed cases were excluded from the sample (Table II).

Table II. Average tattoo lightening with the R20 method versus the conventional treatment method

Tattoo type	R20 method Lightening (%)		Conventional method Lightening (%)	
Professional (n = 8)				
Mean ± SD	88 ± 18		18 ± 8	
Median	96		15	
Amateur	(n = 10)	(n = 7)*	(n = 10)	(n = 7)*
Mean ± SD	84 ± 20	96 ± 7	26 ± 12	32 ± 6
Median	96	100	28	35

*Indicates data excluding the 3 re-tattooed cases.

In contrast, none of the tattoos treated with the conventional method were completely cleared, and lightening was much less than with the R20 method. The average lightening for professional tattoos was only 18% and for amateur tattoos was 26%. Even excluding the 3 re-tattooed subjects, conventional treatment yielded average lightening of only 32% for amateur tattoos (Table II).

For all 18 tattoos, lightening was greater on the R20 half. The difference in lightening response was large (mean 70% for professional; 59% for amateur), and statistically significant ($P < .01$). No tattoo treated with the conventional method received a lightening score higher than 2, whereas 89% of tattoos treated with the R20 method received a score higher than 2 (Fig 2).

The tattoos in this study were black, blue, or green, all of which responded to alexandrite laser treatment. Tattoo age, body location, or skin type had no apparent effect on efficacy.

No scarring or textural changes, infection or postinflammatory hyperpigmentation occurred. Transient mild hypopigmentation occurred in one amateur tattoo of a patient with skin type IV, which had completely resolved 6 months after the treatment.

From self-assessment questionnaires, 90% reported that the R20 method outcome was cosmetically appealing, and 93% found the method very tolerable. Because only a single treatment visit achieved complete or nearly complete tattoo removal, 96% rated the R20 method to be more cost-effective, 87% considered it to be practical, and 97% would recommend the R20 treatment to others.

Figs 3 and 4 illustrate levels of tattoo response to conventional and R20 methods of treatment.

Histologic evaluation

Immediately after conventional single-pass laser treatment method, heavy pigment load remained (score 1 or 2), at dermal depth ranging greatly from

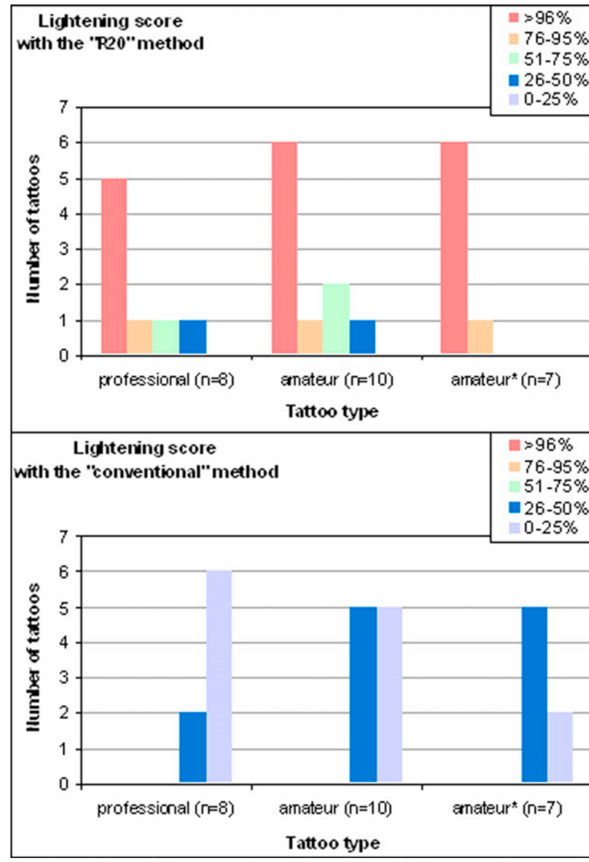

Fig 2. Comparison of lightening response between the two methods for professional and amateur tattoos. *Asterisk* indicates data excluding the 3 re-tattooed cases.

400 to 1500 μm. Pigment density was much greater in the professional and re-tattooed amateur tattoos than in amateur tattoos. Laser-altered pigment was observed in the superficial dermis, while unaltered deposits of dense pigment were present, mainly in perivascular location, at greater depths (mid and deep dermis). The altered superficial pigment granules were brown or gray, less discrete, lacy, and seen extracellularly or within damaged cells. Cells that did not contain tattoo pigment did not appear to be altered. Numerous vacuoles ranging from 20 to 50 μm in diameter were observed in the dermis, sometimes lined by cellular debris or altered pigment. There was mild edema, vascular congestion, and occasional extravasation. There was a mild neutrophilic cell infiltration with occasional eosinophils. Epidermis, hair follicles, sweat and sebaceous glands, nerves and lymphatic vessels appeared normal.

After the R20 method, there was less tattoo pigment, with more pronounced and deeper skin injury. Little or no pigment (score 4) was seen in 72% of the samples. For the remaining samples, pigment scores were 2 and 3 (26%-75% reduction). There was

Fig 3. Five-year professional tattoo on deltoid of patient with skin type III. **A**, Before treatment. **B**, Three months after laser treatment session. *Upper part*: Conventional method. *Lower part*: R20 method, clearance.

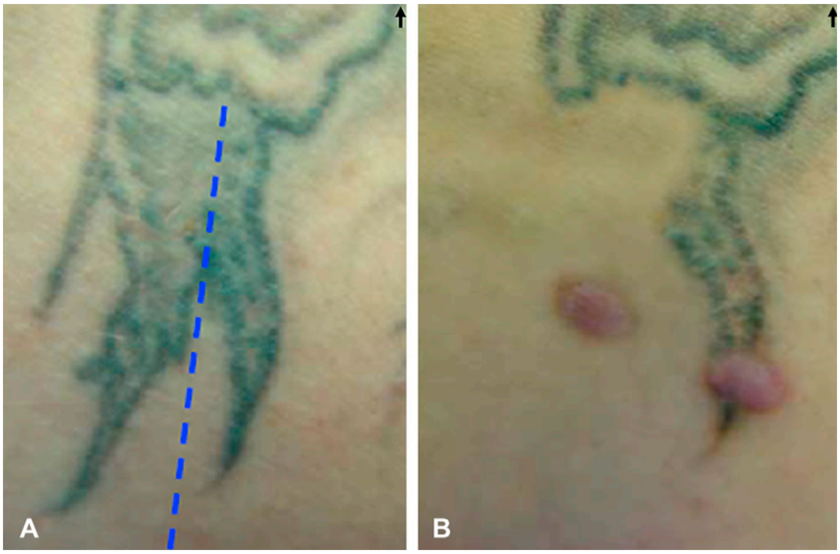

Fig 4. Five-year professional tattoo on back of patient with skin type III. The two round scars are biopsy sites and are not due to laser treatment. **A**, Before treatment. **B**, Three months after laser treatment session. *Right part*: Conventional method. *Left part*: R20 method, clearance.

a gradient of pigment loss with depth. Pigment alterations occurred at a greater depth, including reticular dermis. Adjacent nonpigmented cells were intact. Occasionally, traces of deep, intact aggregated pigment were noticed; the 3 re-tattooed samples had remaining deposits of aggregated pigment in the dermis. Focal homogenization of collagen bundles was noted at the margin of the dermal vacuoles. Otherwise, collagen, elastin, and dermal cells appeared normal. There was vascular stasis and occasionally complete damage of vessel walls with associated extensive extravasation and intercellular edema. Myxoid denaturation around deep eccrine glands was observed in one sample. There was perivascular, vascular, and occasionally adnexal neutrophilic infiltration. Eosinophilic infiltration was seen in one sample. Repeated laser exposures produced focal subepidermal blisters and occasional separation at the dermoepidermal junction. There was localized epidermal necrosis in darker skin phototypes.

DISCUSSION

This study shows that multiple passes of Q-switched laser treatment given about 20 minutes apart (R20 method) are far more effective than conventional Q-switched laser treatment for removal of both amateur and professional tattoos. Extensive tattoo pigment changes were produced at greater skin depth than conventional single-pass laser treatment, with somewhat greater epidermal injury and more purpura. Despite this, the R20 method was safe and did not cause more side effects compared with conventional one-pass laser treatment.

There was a high degree of patient satisfaction in this study because the R20 method is able to completely or nearly completely remove most tattoos in a single treatment session. The only disadvantage appears to be the much longer time required for a treatment session. With 3 intervals of 20 minutes each and additional anesthesia in some patients, the R20 method adds at least a full hour to the treatment session time. In practice, this disadvantage might be minimized by time-sharing the laser treatment room among several patients.

The exact mechanism(s) by which the R20 method is more effective remains unknown. There is clearly a stronger interaction with tattoo ink in the deep dermis, which we hypothesize is related to the influence of immediate whitening. Laser-induced immediate whitening due to gas bubble formation apparently limits penetration of laser light into the deeper dermis. The superficial dermal gas bubbles dissolve over about 20 minutes, such that a subsequent pulse can penetrate deeper after whitening has faded. The skin appears white for the same reason that foams are white: strong optical scattering is produced by gas bubbles, which limits optical penetration. Immediate whitening follows a similar process of cavitation and residual bubble formation that occurs around laser-pumped nanoparticles, including melanosomes and colloidal gold particles within cells, which are similar to tattoo ink particles.[18] We observed that much less immediate whitening occurs with each subsequent laser pass during the R20 method, such that deeper optical penetration is apparently possible. We hypothesize that each pass in the R20 method treats a successively deeper layer of dermis, up to some limit that remains to be established. Potentially, the anatomic depth of a tattoo may be strongly correlated therefore with the number of passes required in the R20 method for removal of that particular tattoo.

Further research on this new method of tattoo removal should be pursued. In the present study, we observed very good results with 4 consecutive laser exposures at a fluence of 5.5 J/cm^2, 3-mm spot size, 100-nanosecond pulse duration, and 20-minute delay time. However, these parameters are undoubtedly not ideal. In general, higher laser fluence is more effective. Larger laser spot size is associated with better tattoo clearance, at a given fluence. For black ink tattoos that absorb strongly at all available Q-switched laser wavelengths, the Nd:YAG (1064 nm) laser tends to perform better, as a result of greater penetration depth. It is also well established that shorter pulse duration, particularly when comparing picosecond to nanosecond laser pulses, is more efficient for tattoo removal.[10,14,19] Presumably, this and other knowledge from previous tattoo removal studies is applicable to improving the R20 method. Other parameters that we did not address in this study also deserve further investigation. For example, an increase in laser fluence between consecutive exposures could allow for deeper penetration of the laser beam in the dermis. Also, we did not study multiple treatment sessions using the R20 method nor did we compare it with 4 conventional treatment sessions.

In summary, we describe a much more effective method for laser removal of tattoos in a single treatment session, by means of existing Q-switched laser technology. A very large number of people have unwanted tattoos, but do not pursue laser treatment because of expense and uncertainty.[20] We hope that delayed, multiple-pass laser treatment may significantly change that situation.

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